UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/718,997	11/21/2003	Ning Wei	KCX-691 (18379)	9089

22827 7590 08/06/2008

DORITY & MANNING, P.A.
POST OFFICE BOX 1449
GREENVILLE, SC 29602-1449

EXAMINER	
DIRAMIO, JACQUELINE A	
ART UNIT	PAPER NUMBER
1641	
MAIL DATE	DELIVERY MODE
08/06/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/718,997	WEI ET AL.	
	Examiner	Art Unit	
	Jacqueline DiRamio	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-31* is/are pending in the application.

4a) Of the above claim(s) *20-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-19 and 29-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 April 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Applicant's amendments to claim 19 are acknowledged, as well as the cancellation of new claims 1 – 13 and addition of new claims 29 - 31.

Currently, claims 14 – 19 and 29 – 31 are pending and under examination. Claims 20 – 28 are acknowledged as withdrawn, as drawn to a non-elected invention.

Withdrawn Objections

The previous objection to claim 19 is withdrawn in view of Applicant's amendments filed April 11, 2008.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 14 – 16 and 29 – 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boehringer et al. (US 7,144,742) in view of Behnke et al. (US 5,573,921).

Boehringer et al. teach a lateral flow (flow-through) assay device for detecting the presence or quantity of an analyte residing in a test sample, said lateral flow assay device comprising a porous membrane in communication with a labeled reagent (optical detection probes) conjugated with a specific binding member, such as a first antibody, specific for the analyte, said porous membrane defining:

a barrier (competitive) zone 16a that contains a second antibody immobilized on said porous membrane that can be complexed to an antigen containing a label (optically detectable substance), said antigen being identical to or an analog of the analyte and said label being capable of producing a signal; and

a detection zone 16b and 16c within which a third antibody is immobilized that is configured to bind to complexes formed between the analyte and said conjugated labeled reagent to produce a first detection signal, said third antibody also being configured to bind to said antigen from said barrier zone to produce a second detection signal, wherein the amount of analyte within the test sample is determined from said detection signals (see Figure 1; and column 3, lines 14-45; column 5, lines 45-59; column 9, lines 51-67; column 10, lines 1-4 and lines 34-64; and column 11, lines 1-62).

However, Boehringer et al. fail to teach that the immobilized antibody in the barrier (competitive) zone is complexed to the antigen containing the optically detectable substance prior to the application of test sample to the device.

Behnke et al. teach a test strip device for determining the amount of analyte in a sample using immunochemical displacement. The test strip device contains at least one immobilized antibody, wherein the antibody is bound to an analyte analog (tracer) prior to application of test sample to the device. The bound analyte analog (tracer) can also include an attached dye (molecule or particle), such that the area of the test strip comprising the immobilized antibody and tracer can be directly visualized even before beginning the test. A sample containing an analyte of interest is applied to the test strip device, which results in the analyte competing with the bound tracer for binding to the immobilized antibody. As analyte concentration increases, tracer containing the attached dye becomes displaced from the immobilized antibody, and the reduction in the dye previously visualized in the area of immobilized antibody can be utilized to determine the amount of analyte in the sample (see Figures 12a and 12b; column 5, lines 19-67; column 6, lines 1-33 and lines 52-56; column 7, lines 9-27; column 13, lines 51-53).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include with the device of Boehringer et al. the binding of the antigen containing the optically detectable substance to the immobilized antibody of the barrier zone prior to application of the test sample as taught by Behnke et al. because Behnke et al. teach the benefit of binding an analyte analog attached to a dye to an immobilized antibody on a test strip prior to application of a test sample containing an analyte of interest, wherein the analyte competes for binding with the bound analyte analog, because the bound analyte analog attached to the dye allows for directly

visualizing the area of the test strip comprising the immobilized antibody (i.e. barrier zone) even before beginning the test, and also allows for utilizing the reduction in the dye from the area of immobilized antibody after applying the test sample in determining the amount of analyte in the sample.

With respect to Applicant's claims 15 and 16, Boehringer et al. teach that the labels can comprise a visual label, such as a dyed latex bead, or a luminescent compound (see paragraph [0090]).

With respect to Applicant's claims 29 and 30, Boehringer et al. teach that the intensity of the signal at the barrier zone is at its maximum when no analyte is present, and that the conjugated labeled reagent is capable of binding to the antigen within the barrier zone to produce a signal (see column 10, lines 52-67; and column 11, lines 1-44).

With respect to Applicant's claim 31, the device set-up of Boehringer et al., wherein the barrier zone comprises a first antibody for the analyte, the detection zone comprises a second antibody for the analyte/antigen, and the analyte competes for binding with the labeled antigen in the barrier zone, would allow for the detection signal at the detection zone to reach a maximum value at or near saturation concentration of the analyte within the test sample (see column 10, lines 52-67; and column 11, lines 1-44).

Claim 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over Boehringer et al. (US 7,144,742) in view of Behnke et al. (US 5,573,921), as applied to claim 14 above, and further in view of Polito et al. (US 2004/0018637).

The Boehringer et al. and Behnke et al. references, which were discussed in the 103(a) rejection above, fail to teach that the labels used for the analyte and antigen (detection probes) emit signals at different wavelengths.

Polito et al. teach a method and apparatus for performing a lateral flow assay. The method utilizes detection agents in the form of particles to label an analyte(s) of interest in order to facilitate detection. Different detection agents can be used with different populations of analytes, wherein the different detection agents can comprise fluorescence agents that fluoresce at different wavelengths. The use of two different detection agents facilitates the detection of two different analytes of interest on the same test strip (see Abstract; and paragraphs [0036]-[0041]).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include with the device of Boehringer et al. and Behnke et al. the use of different labels for the antigen and analyte of interest, wherein the labels fluoresce at different wavelengths as taught by Polito et al. because Polito et al. teach the benefit of utilizing different detection reagents, such as fluorescence agents that fluoresce at different wavelengths, in order to detect two different analytes of interest, i.e. the analyte and antigen of Boehringer et al., on the same test strip.

Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Boehringer et al. (US 7,144,742) in view of Behnke et al. (US 5,573,921), as applied to claim 14 above, and further in view of Harris et al. (US 2003/0162236).

Boehringer et al. and Behnke et al. also fail to teach the inclusion of a calibration zone that is configured to produced a calibration signal.

Harris et al. teach a method and test strip for measuring the amount of an analyte of interest in a fluid sample, wherein the test strip includes an application point, a contact region, a sample capture zone, and a control capture zone (calibration zone). The contact region contains analyte-binding particles, which bind to and label the analyte of interest. The sample and control capture zones contain immobilized capture reagents specific for the analyte or analyte-binding particles. When the fluid sample is contacted with the test strip, the fluid sample flows through the contact region, wherein any analyte in the sample can bind to the analyte-binding particles. The sample then flows to the sample and control capture zones, wherein a certain amount of analyte-binding particles bind to and are arrested in both the sample and control capture zones. The signals generated in both the sample and control capture zones are determined and compared in order to determine a ratio between 1) the amount of analyte-binding particles arrested in the sample capture zone, and 2) the amount of analyte-binding particles in the control capture zone. This ratio allows for an increased sensitivity and a more accurate determination of the amount of analyte of interest in a test sample, while also compensating for the variations that result from the dynamic nature of the assays (see paragraphs [0002]-[0007] and [0013]).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include with the device of Boehringer et al. and Behnke et al. a control/calibration zone as taught by Harris et al. because Harris et al. teach the benefit of including a control capture zone that generates a control signal with a test strip in order to determine a ratio that compares the signals generated in a sample capture zone (detection zone) and the control capture zone (calibration/control zone) in order to accurately determine the amount of analyte of interest in a test sample with increased sensitivity, while also compensating for the variations that result from the dynamic nature of the assays.

Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Boehringer et al. (US 7,144,742) in view of Behnke et al. (US 5,573,921), as applied to claim 14 above, and further in view of Blatt et al. (US 2005/0196875).

Boehringer et al. and Behnke et al. fail to teach a specific formula for determining the amount of analyte within the test sample utilizing the signals generated in the various detection/barrier zones.

Blatt et al. teach an assay device for detecting an analyte within a test sample. The assay device can utilize two zones for binding to an analyte or particle-linked antibody (label) and providing a detectable signal in response to the bound components. The assay quantitation can be determined by reading the signals produced by the two zones, wherein the sample concentration is a result of a calibration algorithm related to the signals produced in the two zones, which provides for a more

reliable quantitative analyte concentration result. Further, the summation of the detectable signals from the two zones to produce a substantially constant total signal regardless of analyte concentration provides a reference mechanism for accurate assay performance (see Abstract; and paragraphs [0055]-[0057]).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to create a formula or algorithm that utilizes the signals generated in the detection and/or barrier zones of Boehringer et al. and Behnke et al. as taught by Blatt et al. because Blatt et al. teach the benefit of creating an algorithm related to the signals produced by two zones contained on an assay device in order to quantitatively determine the concentration of an analyte in an applied test sample more reliably, wherein the summation of the detectable signals from the two zones can produce a substantially constant total signal regardless of analyte concentration, which provides a reference mechanism for accurate assay performance.

Response to Arguments

Applicant's arguments filed April 11, 2008 have been fully considered but they are not persuasive. Applicant argues (see p13-15) that the combination of Boehringer et al. (US 7,144,742) in view of Behnke et al. (US 5,573,921) in order to arrive at Applicant's instant invention is misplaced and contrary to the teachings of the references because: 1) the modification to Boehringer et al. to include the antibody/antigen complex at the "barrier zone" would completely fail to fulfill its intended function because it would no longer be able to bind to the labeled binding member; 2)

no perceived benefit would exist for "visualizing the area of the test strip even before beginning the test;" and 3) the systems of Boehringer et al. and Behnke et al. are so vastly different, one of ordinary skill in the art would not have found it obvious to make the proposed combination. However, these arguments are not found persuasive.

With respect to Applicant's first argument, the Boehringer et al. reference teaches a device comprising a porous membrane in communication with a labeled reagent (optical detection probes) conjugated with a specific binding member, such as a first antibody, specific for the analyte, said porous membrane defining:

a barrier (competitive) zone 16a that contains a second antibody immobilized on said porous membrane that can be complexed to an antigen containing a label (optically detectable substance), said antigen being identical to or an analog of the analyte and said label being capable of producing a signal; and

a detection zone 16b and 16c within which a third antibody is immobilized that is configured to bind to complexes formed between the analyte and said conjugated labeled reagent to produce a first detection signal, said third antibody also being configured to bind to said antigen from said barrier zone to produce a second detection signal, wherein the amount of analyte within the test sample is determined from said detection signals (see Figure 1; and column 3, lines 14-45; column 5, lines 45-59; column 9, lines 51-67; column 10, lines 1-4 and lines 34-64; and column 11, lines 1-62). The device of Boehringer et al. allows for the second antibody immobilized in the barrier zone to bind to the labeled antigen, wherein the concentration of analyte within the sample provides for competition in the barrier zone, i.e. the sample analyte and labeled

antigen compete for binding to the second antibody immobilized within the barrier zone (see column 11, lines 3-31). Therefore, it is unclear why the device of Boehringer et al. would not function properly or fail to perform its intended function if the labeled antigen is already bound to the second antibody of the barrier zone, when the function of the barrier zone is to compete for binding to the immobilized antibody, and this would occur either way.

With respect to Applicant's second argument, the motivation for combining the Boehringer et al. reference with Behnke et al. in order to arrive at the instant device, which includes the labeled antigen immobilized within the barrier zone prior to application of the test sample, comprises the ability to directly visualize the area of the test strip comprising the immobilized antibody (i.e. barrier zone) even before beginning the test, and also allows for utilizing the reduction in the dye from the area of immobilized antibody after applying the test sample in determining the amount of analyte in the sample. Therefore, these benefits or advantages taught by the Behnke et al. reference provide motivation for combining the two references. The fact that Applicant fails to perceive a benefit or has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

Finally, with respect to Applicant's final argument, the systems of Boehringer et al. and Behnke et al. are not considered to be so vastly different such that one of ordinary skill in the art would not have found it obvious to make the combination as

discussed above. In particular, both references teach test strips for use in determining an analyte of interest in a sample, wherein the test strips utilize at least one competitive zone for competing for binding to the analyte and a labeled antigen/analog to analyte (see Boehringer et al: Figure 1; and column 3, lines 14-45; column 5, lines 45-59; column 9, lines 51-67; column 10, lines 1-4 and lines 34-64; and column 11, lines 1-62; and Behnke et al: Abstract; Figures 12a and 12b; column 5, lines 19-67; column 6, lines 1-33 and lines 52-56; column 7, lines 9-27; column 13, lines 51-53). Applicant appears to be arguing that the references comprise nonanalogous art. However, it has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). Therefore, the combination of Boehringer et al. in view of Behnke et al. is considered applicable and is maintained in order to arrive at Applicant's claimed invention.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jacqueline DiRamio whose telephone number is 571-272-8785. The examiner can normally be reached on M-F 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jacqueline DiRamio/
Examiner, Art Unit 1641

/Mark L. Shibuya, Ph.D./
Supervisory Patent Examiner, Art Unit 1641